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Ethynylation process

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Case 21364Ethynylation process

The present invention relates to an ethynylation process. More particularly, the present invention relates to a process for the preparation of acetylenically unsaturated
5 alcohols (propargyl alcohol or 1-monosubstituted or 1,1-disubstituted derivatives thereof) in which process a ketone is reacted with ethine in the presence of ammonia and an alkali hydroxide wherein the molar ratio of alkali hydroxide to ketone is less than 1 : 200.

The reaction products are of use as intermediates in the synthesis of many useful end products, inter alia in the field of vitamins and carotenoids. For example, one such useful
10 intermediate is dehydrolinalool, which itself can be converted via citral to isophytol and β -ionone, themselves being known starting materials for vitamin E and vitamin A, respectively.

The preparation of acetylenically unsaturated alcohols by reaction of a ketone with ethine in the presence of ammonia and an alkali hydroxide is known from e.g., DE-PS 1
15 232 573. According to that patent specification the ethynylation reaction is carried out at a temperature of from -40°C to $+40^{\circ}\text{C}$ in the presence of an alkali hydroxide and a molar ratio of alkali hydroxide to ketone of 1:10 to 1:200. As is apparent from technical data provided in the specification of DE-PS 1 232 573 the yield of ethynylation product decreased when the amount of alkali hydroxide was reduced.

20 In accordance with the present invention it has surprisingly been found that acetylenically unsaturated alcohols can be obtained in superior yield within short reaction time by reacting a ketone with ethine in the presence of ammonia and an alkali hydroxide when the molar ratio of alkali hydroxide to ketone is less than 1 : 200. The use of such low amounts of alkali hydroxide not only reduces the amount of salt to be disposed of as waste.

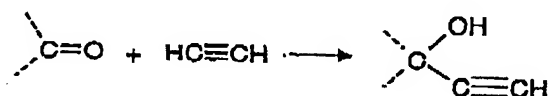
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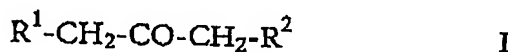
It has been found that by the use of reduced amounts of alkali hydroxide catalyst less diol by-product is formed. Since the formation of diol by-products increases at elevated temperature the reaction in accordance with the invention can thus be carried out at higher temperature, i.e. without cooling, while keeping the diol by-product formation at low levels. Suitably, the ethynylation reaction is carried out at temperatures between about room temperature and about 35 °C.

In a preferred embodiment of the invention, the molar amount of the reactants is about 3 to 6 moles of ketone per mole of ethine. The process in accordance with this preferred embodiment can suitably be carried out by providing and sustaining an adequate ethine pressure in the reaction vessel.

In accordance with the process of the present invention any aldehyde or ketone with which ethine is known to react to form an acetylenically unsaturated alcohol may be used. i.e. according to the equation



, the unspecified moieties attached to the "central" carbon atom by the dotted lines being those featured in known aldehydes and ketones or in any other aldehydes and ketones which can be produced analogously. The simplest compound with which ethine can be reacted in accordance with the process of the present invention is formaldehyde, H_2CO . The aldehyde or ketone may be one of those of formula " $\text{R}^5\text{-CO-R}^6$ " as defined in German Offenlegungsschrift 2 018 971, the contents of which are incorporated herein for reference purposes. Preferably, the starting carbonyl compound is a ketone of the general formula



wherein each of R^1 and R^2 , independently, signifies hydrogen alkyl, alkenyl, cycloalkyl-alkyl, cycloalkyl-alkenyl, cycloalkenyl-alkyl or cycloalkenyl-alkenyl, each of the last four mentioned groups being optionally substituted on its cycloalkyl or cycloalkenyl ring, as appropriate, by one to three methyl or ethyl groups, the total number of carbon atoms, including those of the $\text{-CH}_2\text{-CO-CH}_2\text{-}$ moiety, conveniently not exceeding 40.

In the above definition of the ketones of the general formula I an alkyl group signified by R^1 and/or R^2 suitably contains up to 22 carbon atoms and may be straight chain or branched, which also applies to the alkenyl group. Said alkenyl group, in addition, may feature up to 4 double bonds. The cycloalkyl-alkyl, cycloalkenyl-alkyl, cycloalkyl-
 5 alkenyl or cycloalkenyl-alkenyl group signified by R^1 and/or R^2 features a cycloalkyl or cycloalkenyl ring, as appropriate, which has from 5 to 12 ring members; the alkyl or alkenyl part of such group can contain from 1 to 8 carbon atoms and be straight chain or branched, and in the case of alkenyl as part of such group this can feature up to 4 double bonds. Furthermore, and as also indicated in the definition of formula I, the cycloalkyl or
 10 cycloalkenyl ring part of such groups is either unsubstituted or is substituted by one, two or three methyl or ethyl groups, whereby in the case of di- or trisubstitution the substituents can be the same (methyl or ethyl) or different (a mixture of methyl and ethyl substituents). A particularly preferred optionally substituted cycloalkenyl group (as part of cycloalkenyl-alkyl or cycloalkenyl-alkenyl) is the well known 2,6,6-trimethyl-1-cyclohexen-
 15 1-yl group.

Of particular interest is the process of the present invention when applied to the ethynylation of methyl ethyl ketone, 6-methyl-5-hepten-2-one, 6-methyl-5-octen-2-one, hexahydropseudoionone (6,10-dimethyl-2-undecanone), 4-(2,6,6-trimethyl-1-cyclohexen-
 20 1-yl)-3-buten-2-one and 6,10,14-trimethyl-2-pentadecanone (all ketones of formula I), and also to the ethynylation of methylglyoxal dimethylacetal $[CH_3COCH(OCH_3)_2]$, not a ketone of the formula I, but nonetheless a ketone amongst many others which can be reacted with ethine in accordance with the process of the present invention. Of these specifically named ketones 6-methyl-5-hepten-2-one is a particularly preferred ketone which can be reacted with ethine by the process of the present invention; the product in
 25 this case is dehydrolinalool.

The process of the present invention can be carried out in a manner known per se for the ethynylation of ketones. Typically, for batchwise operation, defined amounts of alkali hydroxide solution and ketone and ketone ethine is fed into a reactor. The alkali hydroxide may be sodium or potassium hydroxide with potassium hydroxide being the
 30 preferred catalyst. The reactor is then sealed and inertized by repeated filling with ammonia and venting. Finally, a defined amount of ammonia is filled into the reactor. Ethine is then added in the desired amount with stirring to start the reaction. During the reaction further ethine may be added semi-continuously to sustain a constant ketone : ethine ratio. The reaction in accordance with the present invention can be carried out also

in a continuous manner, e.g. by continuous addition of an ethine/ammonia mixture together with the ketone and aqueous alkali hydroxide solution into a plug-flow reactor.

The following Examples illustrate the invention further.

Example 1

5 Ethynylation of 6-methyl-5-hepten-2-one to produce dehydrolinalool :

796 mg of potassium hydroxide (45 % (wt/vol) aqueous solution) and 194.5 g of 6-methyl-5-hepten-2-one (MH) were added into a reactor. The molar ratio KOH : MH was thus 1 : 250. After inertisation of the reactor, 369 g of ammonia were added. Ethine was fed into the reactor to provide a pressure of 16.1 bar at 30 °C, corresponding to 21 % (wt/vol) of ethine in the ammonia ethine mixture. The contents of the reactor were stirred by gas stirring. Samples were taken at various time intervals. After 5 hours the reaction was finally stopped. The results are tabulated in Table 1 below:

Table 1 : Product quality vs. time

	5 min	1 hr	2 hrs	5 hrs
MH	29.2	4.1	2.5	2.3
DLL	67.6	92.9	94.3	94.1
Diol	1.0	1.4	1.5	1.7

MH : 6-methyl-5-hepten-2-one (methyl heptenone)

DLL : 3,7-dimethyl-6-octen-1-in-3-ol (dehydrolinalool)

Diol : diol by-product

20 Example 2

Ethynylation of hexahydropseudoionone to produce 3,7,11-trimethyl-1-dodecin-3-ol:

In analogy to Example 1, 387 mg of potassium hydroxide (45 % (wt/vol) aqueous solution), 153.8 g of hexahydropseudoionone and 360 g of ammonia and ethine were reacted at 16.3 bar und 30 °C. The molar ratio KOH : hexahydropseudoionone was thus 1 : 250. The results are tabulated in Table 2 below:

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Table 2 : Product quality vs. time

	5 min	1 hr	2 hrs	5 hrs
HPI	29.4	4.0	3.1	3.1
C15-AA	68.5	93.7	94.2	94.4
Diol	0.4	0.6	0.6	0.8

HPI : 6,10-dimethyl-2-undecanone (hexahydropseudoionone)

C15-AA : 3,7,11-trimethyl-1-dodecin-3-ol (C₁₅-acetylenic alcohol)

5 Diol : diol by-product

Example 3

Ethynylation of 6,10,14-trimethylpentadeca-2-one to produce dehydroisophytol :

10 In analogy to Example 1, 358 mg of potassium hydroxide (45 % (wt/vol) aqueous solution), 192.3 g of hexahydropseudoionone and 351 g of ammonia and ethine were reacted at 16.8 bar und 30 °C. The molar ratio KOH : 6,10,14-trimethylpentadeca-2-one was thus 1 : 250. The results are tabulated in Table 3 below:

Table 3 : Product quality vs. time

	5 min	1 hr	2 hrs	5 hrs
C18-K	32.7	4.3	3.1	2.6
DIP	64.7	93.3	94.2	94.5
Diol	0.4	0.6	0.6	0.8

15

C18-K: 6,10,14-trimethyl-2-pentadecanone (C₁₈-ketone)

DIP : 3,7,11,15-tetramethyl-1-hexadecin-3-ol (dehydroisophytol)

Diol : diol by-product

20 Example 4

Ethynylation of 6-methyl-5-octen-2-one to produce ethyl dehydrolinalool :

In analogy to Example 1, 593 mg of potassium hydroxide (45 % (wt/vol) aqueous solution), 166.8 g of 6-ethyl-5-octen-2-one and 381 g of ammonia and ethine were reacted

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at 16.1 bar und 30 °C. The molar ratio KOH : 6-methyl-5-octen-2-one was thus 1 : 250.
The results are tabulated in Table 4 below:

Table 4 : Product quality vs. time

	5 min	1 hr	2 hrs	5 hrs
EH	29.2	3.5	2.3	2.3
EDLL	68.3	93.9	95.0	95.0
Diol	0.5	0.8	0.9	1.1

- 5 EH : 6-methyl-5-octen-2-one (ethyl heptenone)
EDLL : 3,7-dimethyl-6-nonen-1-in-3-ol (ethyl dehydrolinalool)
Diol : diol by-product

Example 5

- 10 Ethynylation of methyl ethyl ketone to produce ethinyl butinol :

In analogy to Example 1, 740 mg of potassium hydroxide (45 % (wt/vol) aqueous solution), 153.7 g of methyl ethyl ketone and 388 g of ammonia and ethine were reacted at 16.0 bar und 30 °C. The molar ratio KOH : methyl ethyl ketone was thus 1 : 359.
The results are tabulated in Table 5 below:

- 15 Table 5 : Product quality vs. time

	5 min	1 hr	2 hrs	5 hrs
MEK	25.8	2.9		
EBI	73.6	96.3		
Diol	0.3	0.4		

MEK : methyl ethyl ketone

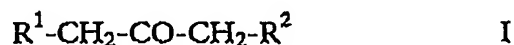
EBI : ethinyl butinol

Diol : diol by-product

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What is claimed is :

1. A process for the preparation of acetylenically unsaturated alcohols which comprises reacting a ketone with ethine in the presence of ammonia and an alkali hydroxide, wherein the molar ratio of alkali hydroxide to ketone is less than 1 : 200.
- 5 2. A process as in claim 1 wherein the molar ratio of ketone : ethine is from about 3 : 1 to about 6 : 1.
3. The process as in claim 2 which is carried out while sustaining the desired ketone : ethine ratio by providing an adequate ethine pressure in the reaction vessel.
4. A process according to any one of claims 1 to 3, wherein the carbonyl compound is a
10 ketone of the general formula



- wherein each of R^1 and R^2 , independently, signifies hydrogen, alkyl, alkenyl, cycloalkyl-
15 alkyl, cycloalkyl-alkenyl, cycloalkenyl-alkyl or cycloalkenyl-alkenyl, each of the last four mentioned groups being optionally substituted on its cycloalkyl or cycloalkenyl ring, as appropriate, by one to three methyl or ethyl groups.
5. A process as in claim 4 wherein the ketone is methyl ethyl ketone, 6-methyl-5-hepten-2-one, 6-methyl-5-octen-2-one, hexahydropseudoionone, 4-(2,6,6-trimethyl-1-cyclohexen-
20 1-yl)-3-buten-2-one, or 6,10,14-trimethyl-2-pentadecanone.
 6. A process as in any one of claims 1 to 4 wherein the ketone is methyl ethyl ketone.
 7. A process as in any one of claims 1 to 4 wherein the ketone is 6-methyl-5-hepten-2-one.
 8. A process as in any one of claims 1 to 3 wherein the ketone is methylglyoxal dimethylacetal.
 9. A process as in any one of claims 1 to 4 wherein the ketone is 4-(2,6,6-trimethyl-1-cyclohexen-1-yl)-3-buten-2-one.
 10. A process as in any one of claims 1-8 wherein the molar ratio of alkali hydroxide : ketone is about 1 : 250.

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11. A process as in any one of claims 1-9 wherein the alkali hydroxide is potassium hydroxide.

12. The invention as particularly described hereinbefore, especially with reference to the Examples.

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